

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Eisenschenk on 11/3/11.

Subsequent to allowance, Ms. Loke (Mr. Eisenschenk's secretary) telephoned the Examiner to correct issues with regard to Claims 82 and 83. To wit, the claims should read ...a mutein thereof, and hence, the presence corrected notice is supplied to correct the language of the claims. In addition, Ms. Loke supplied a new copy of the amendment which was forwarded the Examiner originally, because it appears that the office systems lost the document which was originally attached.

The application has been amended as follows:

**IN THE CLAIMS:**

1. Please AMEND Claim 77, as follows:

77. A method of expressing a gene of interest in a Chinese Hamster Ovary (CHO) cell comprising

culturing a CHO cell comprising a vector under conditions that allow for the expression of said gene of interest,

said vector comprising a promoter, a DNA encoding at least one gene of interest and one or more chromatin insulators consisting of SEQ ID NO:

1 and

wherein said CHO cell expresses the gene of interest.

2. Please AMEND Claim 78 as follows:

78. The method according to claim 77, wherein the vector further comprises ~~at least one DNA element selected from:~~

a) ~~—an enhancer or a functional expressing enhancing fragment thereof;~~

b) ~~—a promoter domain or a functional expression promoting fragment thereof; or~~

e) ~~—a DNA sequence coding for one or more polypeptides of interest.~~

3. Please AMEND Claim 80 as follows:

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80. The method according to claim [[78]]77, wherein the DNA ~~sequence~~  
~~is coding for~~encodes more than one polypeptide of interest through a  
polycistronic mRNA.

4. Please AMEND Claim 82 as follows:

82. The method according to claim [[78]]77, wherein the promoter is  
selected from the group consisting of cellular or a viral promoter[[/]], a  
phage promoter[[s]], ~~such as~~ mCMV-IE1, mCMV-IE2, hCMV, SV40, RSV,  
T7, T3, and[[or]] a functional expression promoting fragment thereof.

5. Please AMEND Claim 83 as follows:

83. The method according to claim [[78]]77, wherein the gene of interest  
encodes a polypeptide of interest ~~is~~ selected from the group consisting of  
FSH, LH, CG, TSH, a growth hormone, an interferon, TNF binding protein  
I, TNF binding protein II, IL-18BP, IL-6, IFNAR1, LIF<sub>1</sub> [[or ]]a mutein[[s]]  
thereof, a fragment[[s]] thereof, a functional derivative[[s]] thereof, and a  
fusion protein[[s]] thereof.

6. Please AMEND Claim 84 as follows:

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84. The method according to claim [[78]]77, wherein the gene of interest encodes a polypeptide of interest ~~is~~-selected from the group consisting of EPO, G-CSF, GM-CSF, a chain of a humanized antibody, a cytokine, a coagulation factor, etanercept, tPA, an integrin, or a mutein thereof, a fragment thereof, a functional derivative thereof, and a fusion protein thereof.

5. Please AMEND Claim 85 as follows:

85. The method according to claim [[78]]77, wherein the gene of interest encodes a polypeptide of interest ~~is~~-selected from the group consisting of adenosine deaminase (ADA), aminoglycoside phosphotransferase (neo), dihydrofolate reductase (DHFR), hygromycin-B-phosphotransferase (HPH), thymidine kinase (tk), xanthine-guanine phosphoribosyltransferase (HPH), multiple drug resistance gene (MDR), ornithine decarboxylase (ODC) [[and]]N-(phosphonacetyl)-L-aspartate resistance (CAD), puromycin acetyltransferase (PAC), galactokinase, human folate receptor, [[or]]and a reduced folate carrier[s].

6. Please AMEND Claim 86 as follows:

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86. The method according to claim [[78]]77, wherein the gene of interest encodes a polypeptide of interest ~~is selected from the group consisting of~~ luciferase, green fluorescent protein, alkaline phosphatase, [[and]] horseradish peroxidase<sub>2</sub> [[or]] and a combination[[s]] thereof.

7. Please AMEND Claim 87 as follows:

87. The method according to claim [[78]]77, wherein one insulator is positioned upstream and one insulator is positioned downstream of the ~~DNA sequence coding for a polypeptide of interest~~ gene of interest.

8. Please AMEND Claim 88 as follows:

88. The method according to claim [[78]]77, wherein at least two insulators are positioned upstream and downstream of the gene of interest ~~a DNA sequence coding for a polypeptide of interest~~, respectively.

9. Please AMEND Claim 89 as follows:

89. The method according to claim [[78]]77, wherein at least two protein encoding DNA coding sequences are positioned between the insulators.

10. Please AMEND Claim 90 as follows:

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90. The method according to claim [[78]]89, wherein the at least two coding sequences code for subunits of a multimeric protein.

11. Please AMEND Claim 91 as follows:

91. The method according to claim 90, wherein the multimeric protein is a hormone comprising a first subunit that is the alpha chain and a second subunit that is the beta chain of a hormone selected from the group consisting of: human FSH, human LH, human TSH, and human CG.

12. Please AMEND Claim 93 as follows:

93. The method according to claim 77, wherein said CHO cell simultaneously expresses two or more genes of interest from the vector.

The following is an examiner's statement of reasons for allowance:

Applicant's amendment is now claiming the single insulator and is therefore allowable over the prior art, and the examiner's amendment, agreed to by Applicant, overcomes all other issues. In addition, because no one had delineated in the prior art whether or not the intervening sequences were required to have a particular spacing for binding the proteins properly,

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similar to other elements, like bacteriophage operator/repressor the spacing was not known whether it would be influenced for its action as an insulator. Hence, the claimed sequence is commensurate with an advancement in the Art.

Claims 77-95 are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/ROBERT M KELLY/  
Primary Examiner, Art Unit 1633